Amendments to the Specification

The paragraph beginning at page 4, line 7, has been amended as follows:

In addition, when a peptide fingerprint of an unknown protein is obtained, it can be compared to a database of known proteins to assist in the identification of the unknown protein using mass spectrometry (Henzel, W. J. et al., *Proc. Natl. Acad. Sci. USA* 90:5011-5015 (1993); Fenyo, D. et al., *Electrophoresis* 19:998-1005 (1998)). A variety of computer software programs to facilitate these comparisons are accessible via the Internet, such as Protein Prospector (Internet site: prospector.uscf.edu), MultiIdent (Internet site: ~~www.~~expasy.ch/sprot/multiident), PeptideSearch (Internet site: ~~www.~~mann.embl-heiedelberg.de...deSearch/FR_PeptideSearchForm), and ProFound (Internet site: ~~www.~~chait-sgi.rockefeller.edu/cgi-bin/prot-id-frag). These programs allow the user to specify the cleavage agent and the molecular weights of the fragmented peptides within a designated tolerance. The programs compare these molecular weights to protein molecular weight information stored in databases to assist in determining the identity of the unknown protein. Accurate information concerning the number of fragmented peptides and the precise molecular weight of those peptides is required for accurate identification. Therefore, increasing the accuracy in determining the number of fragmented peptides and their molecular weight should result in enhanced likelihood of success in the identification of unknown proteins.

The paragraph beginning at page 4, line 22, has been amended as follows:

In addition, peptide digests of unknown proteins can be sequenced using tandem mass spectrometry (MS/MS) and the resulting sequence searched against databases (Eng, J. K. et al., *J. Am. Soc. Mass Spec.* 5:976-989 (1994); Mann, M. et al., *Anal. Chem.* 66:4390-4399 (1994); Taylor, J.A. et al., *Rapid Comm. Mass Spec.* 11:1067-1075 (1997)). Searching programs that can be used in this process exist on the Internet, such as Lutefisk 97 (Internet site: ~~www.~~lsbc.com:70/Lutefisk97), and the Protein Prospector, Peptide Search and ProFound programs described above. Therefore, adding the sequence of a gene and its predicted protein sequence and peptide fragments to a sequence database can aid in the identification of unknown proteins using tandem mass spectrometry.

The paragraph beginning at page 43, line 22, has been amended as follows:

As set forth above, a polypeptide or peptide fingerprint can be entered into or compared to a database of known proteins to assist in the identification of the unknown protein using mass spectrometry (W.J. Henzel et al., *Proc. Natl. Acad. Sci. USA*, 90:5011-5015 (1993); D. Fenyo et al., *Electrophoresis*, 19:998-1005 (1998)). A variety of computer software programs to facilitate these comparisons are accessible via the Internet, such as Protein Prospector (Internet site: prospector.uscf.edu), MultiIdent (Internet site: ~~www.~~expasy.ch/sprot/multiident), PeptideSearch (Internet site: ~~www.~~mann.embl-heiedelberg.de...deSearch/FR_PeptideSearchForm), and ProFound (Internet site: ~~www.~~chait-sgi.rockefeller.edu/cgi-bin/prot-id-frag). These programs allow the user to specify the cleavage agent and the molecular weights of the fragmented peptides within a designated tolerance. The programs compare observed molecular weights to predicted peptide molecular weights derived from sequence databases to assist in determining the identity of the unknown protein.

The paragraph beginning at page 43, line 33, has been amended as follows:

In addition, a polypeptide or peptide digest can be sequenced using tandem mass spectrometry (MS/MS) and the resulting sequence searched against databases (J.K. Eng, et al., *J. Am. Soc. Mass Spec.*, 5:976-989 (1994); M. Mann and M. Wilm, *Anal. Chem.*, 66:4390-4399 (1994); J.A. Taylor and R.S. Johnson, *Rapid Comm. Mass Spec.*, 11:1067-1075 (1997)). Searching programs that can be used in this process exist on the Internet, such as Lutefisk 97 (Internet site: ~~www.~~lsbc.com:70/Lutefisk97), and the Protein Prospector, Peptide Search and ProFound programs described above.

The paragraph beginning at page 47, line 21, has been amended as follows:

As noted above, SVPH-1a, SVPH-1b, and SVPH-1c diverge from the consensus zinc-binding cluster (**HEXXHXXGXXHD**) (SEQ ID NO:31) in the catalytic domain with a Glu to His change at position 333. To analyze these proteins further, DNA and protein sequence multiple alignments of all known mammalian ADAMs (~~www.~~med.virginia.edu/~jag6n/adams) were produced using the PILEUP program from the Wisconsin Package (Wisconsin Package 10.1, Genetics Computer Group, Madison, WI).

Protein multiple alignments were generated using the modified PAM scoring matrix of Gribskov and Burgess (Gribskov, M. et al., *Nucleic Acids Res.*, 14:6745-6763 (1986)) provided in the Wisconsin Package, with gap-open and gap-extend penalties of 30 and 1, respectively. Nucleic acid multiple alignments were generated using a scoring matrix with A, C, G, T matches scoring unity, mismatches scoring zero, and gap-open and gap-extend penalties of 5 and 1 respectively. Unrooted maximum parsimony trees were estimated by the Wisconsin Package implementation of PAUP (version 4.0), starting from multiple alignments produced by PILEUP. PAUP parameters were set to use accelerated transformation character-state optimization with unordered, equally weighted characters.